Amendment to the Claims:

Please cancel claims 1 to 106 and 108 to 123 without prejudice or disclaimer.

Please amend claim 107 and add new claims 124 to 168 as follows.

The following listing of claims is intended to replace all previous claims.

107. (currently amended) An assay for determining the optimal conditions for sterilizing a tissue that contains collagen without adversely ~~affective~~ affecting a predetermined biological characteristic or property thereof, said method comprising ~~the steps of:~~ (i) irradiating collagen under a pre-determined set of conditions effective to sterilize said tissue; (ii) determining the turbidity of said irradiated collagen; and (iii) repeating steps (i) and (ii) with a different pre-determined set of conditions until said turbidity of said irradiated collagen reaches a pre-determined acceptable level.

124. (new) A method for reducing the level of active biological contaminants or pathogens in one or more tissues, said method comprising contacting the tissue with a composition comprising propylene glycol, and irradiating said one or more tissues with gamma radiation for a time effective to reduce the level of active biological contaminants or pathogens in said one or more tissues.

125. (new) A method for reducing the level of active biological contaminants or pathogens in one or more tissues, said method comprising contacting the tissue with at least two stabilizers, wherein one of the stabilizers is propylene glycol and irradiating said one or more tissues with gamma radiation for a time effective to reduce the level of active biological contaminants or pathogens in said one or more tissues.

126. (new) The method of claim 124 or 125 wherein the tissue is hard tissue.

127. (new) The method of claim 126 wherein the hard tissue is selected from the group consisting of bone, demineralized bone matrix, joints, femurs, femoral heads and teeth.

128. (new) The method of claim 124 or 125 wherein the tissue is soft tissue.

129. (new) The method of claim 128 wherein the soft tissue is selected from the group consisting of collagen, connective tissue, epithelial tissue, adipose tissue, bone marrow, ligaments, tendons, nerves, nerve cells, skin grafts, heart valves, portions of brain, cartilage, corneas, arteries and veins.

130. (new) The method of claim 124 or 125 wherein said one or more tissues is a combination of hard and soft tissue.

131. (new) The method of Claim 124 or 125 wherein said one or more tissues is at a temperature below its freezing point during irradiation.

132. (new) The method of claim 131 wherein said one or more tissues is at a temperature of about 0° C to about -196° C during irradiation.

133. (new) The method of claim 131 wherein said one or more tissues is at a temperature of about -50° C to about -78° C during irradiation.

134. (new) The method of claim 124 or 125 wherein said tissue is maintained in an inert atmosphere during irradiation.

135. (new) The method of Claim 124 or 125 wherein said tissue is maintained under vacuum during irradiation.

136. (new) The method according to claim 124 or 125 wherein said irradiation is applied at a rate of at least about 0.3 kGy/hour to at least about 30.0 kGy/hour.

137. (new) The method of claim 124 or 125 wherein the total dose of gamma irradiation is at least about 30 kGy.

138. (new) The method of claim 124 or 125 wherein the total dose of gamma irradiation is at least about 45 kGy.

139. (new) The method of claim 124 or 125 wherein the total dose of gamma irradiation is at least about 50 kGy.

140. (new) The method of claim 124 or 125 wherein the concentration of the stabilizer or propylene glycol is at least about 20 mM to about 1 M.

141. (new) The method of claim 124 or 125 wherein the concentration of the stabilizer or propylene glycol is at least about 100 mM to about 500 mM.

142. (new) The method of claim 125 wherein one of the stabilizers is DMSO.

143. (new) The method of claim 142 wherein the concentration of DMSO is about fifteen (15) to about fifty (50) percent (v/v).

144. (new) The method of claim 125 wherein one of the stabilizers is mannitol.

145. (new) The method of claim 144 wherein the concentration of mannitol is about 150 mM.

146. (new) The method of claim 125 wherein one of the stabilizers is trehalose.

147. (new) The method of claim 125 wherein a combination of three or more stabilizers are contacted with said tissue.

148. (new) The method of Claim 147 wherein three or more stabilizers are selected from the group consisting of DMSO, mannitol and trehalose.

149. (new) The method of claim 124 or 125 further comprising adjusting or maintaining the pH of said one or more tissues prior to irradiation.

150. (new) The method of claim 124 or 125 further comprising reducing the residual solvent content of the tissue prior to irradiation.

151. (new) The method of claim 150 wherein said residual solvent is a non-aqueous solvent.

152. (new) The method of claim 150 wherein said residual solvent is an aqueous solvent.

153. (new) The method of claim 150 wherein said residual solvent content is reduced by a method selected from the group consisting of lyophilization, drying, addition of a second solvent, evaporation, chemical extraction and vitrification.

154. (new) The method of claim 150 wherein said residual solvent content is reduced to about about six (6) to about eight (8) percent.

155. (new) The method of claim 124 or 125 wherein said one or more tissues is glassy or vitrified.

156. (new) The method of claim 124 or 125 further comprising contacting said one or more tissues with at least one compound effective to increase penetration of propylene glycol into said tissue.

157. (new) The method of claim 124 or 125 further comprising contacting said one or more tissues with at least one sensitizer prior to irradiation.

158. (new) The method of claim 157 wherein said sensitizer is selected from the group consisting of psoralen, 3-carboethoxy psoralens, inactines, angelicins, khellins, coumarins, brominated hematoporphyrin, phthalocyanines, purpurins, porphyrins, halogenated or metal atom-substituted derivatives of dihematoporphyrin esters, hematoporphyrin derivatives, benzoporphyrin derivatives, hydrodibenzoporphyrin dimaleimade, hydrodibenzoporphyrin, dicyano disulfone, tetracarbethoxy hydrodibenzoporphyrin, tetracarbethoxy hydrodibenzoporphyrin dipropionamide, doxorubicin, daunomycin, netropsin, BD peptide, S2 peptide, S-303 (ALE compound), hypericin, methylene blue, eosin, fluoresceins, flavins, merocyanine 540, bergapten, SE peptide, Cu^{2+} and Cu^{3+} and combinations thereof.

159. (new) The method of claim 124 or 125 wherein said one or more tissues contains at least one biological contaminant or pathogen selected from the group consisting of viruses, bacteria, yeasts, molds,

fungi, parasites, prions, causative agents of transmissible spongiform encephalopathies and combinations thereof.

160. (new) The method of claim 125, wherein one of the stabilizers is selected from the group consisting of hydroquinonesulfonic acid, sodium formaldehyde sulfoxylate, propyl gallate, coumaric acid, deferoxamine, ergothionine, thiourea, tert-butyl-nitrosobutane, alpha-phenyl-tert-butylnitrone, 5,5-dimethylpyroroline-N-oxide, tert-butylnitrosobenzene, alpha-(4-pyridyl-1-oxide)-N-tert-butylnitrone, 3,5-dibromo-4-nitrosos-benzenesulphonic acid, 6,8-dimercapto-octanoic acid (lipoic acid) alpha thioctic acid, beta thioctic acid, dihydro thioctic acid, bisno thioctic acid tetranor thioctic acid, 6,8-dimercapto-octanoic acid, dihydrolopoate (DL-6,8-dithioloctanoic acid methyl ester), lipoamide, bisonor methyl ester, tetranor-dihydrolipoic acid, omega-3 fatty acids, omega-6 fatty acids, omega-9 fatty acids, furan fatty acids, oleic acids, linoleic acids, arachidonic acids, eicosapentaenoic acids, docasahexaenoic acids, palmitic acids, alpha carotenes, beta carotenes, gamma carotenes, sucrose, glycerol, mannitol, inositol, sorbitol, xylose, glucose, ribose, mannose, fructose, erythrose, threose, idose, arabinose, lyxose, galactose, allose, altrose, gulose, talose, trehalose, arginine, lysine, alanine, valine, leucine, isoleucine, proline, phenylalanine, glycine, serine, threonine, tyrosine, asparagine, glutamine, aspartic acid, histidine, N-acetylcysteine (NAC), glutamic acid, tryptophan, sodium capryl N-acetyl tryptophan, methionine sodium azide, Δ4-desaturase, Δ5-desaturase, Δ6-desaturase, uric acid, 1,3-dimethyluric acid, dimethylthiourea, allopurinol, glutathione, reduced glutathione, cysteine, selenium, chromium, boron, vitamin A, ascorbic acid (vitamin C), sodium ascorbate, palmitoyl ascorbic acid, vitamin E, alpha-tocopherol, beta-tocopherol, gamma-tocopherol, delta-tocopherol, epsilon-tocopherol, zeta-tocopherol, eta-tocopherol, tocopherol acetate, alpha-tocotrienol, chromanol-alpha-C6, 6-hydroxy-2,5,7,8-tetramethylchroma-2 carboxylic acid (Trolox), gelatin, albumin, tris-3-methyl-1-phenyl-2-pyrazolin-5-one (MCI-186), citiolone, puercetin, chrysin, dimethyl sulfoxide (DMSO), piperazine diethanesulfonic acid (PIPES), imidazole, methoxypsoralen (MOPS), 1,2-dithiane-4,5-diol, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), very low density lipoprotein (VLDL), probucol, thimerosal, lazaroid, tirilazad mesylate, proanthenols, proanthocyanidins, ammonium sulfate, Pegorgotein (PEG-SOD), N-tert-butyl-alpha-phenylnitrone (PBN), 4-hydroxy-2,2,6,6-tetramethylpiperidin-1-oxyl (Tempol), Gly-Gly (glycylglycine), Trp-Trp, carnosine (β-alanyl-histidine), anserine (β-alanyl-methylhistidine), Gly-Trp, diosmin, quercetin, rutin, silybin, silidianin, silicristin, silymarin, apigenin, apiin, chrysin, morin, isoflavone, flavoxate, gossypetin, myricetin, biacalein, kaempferol, curcumin, proanthocyanidin B2-3-O-gallate, epicatechin gallate, epigallocatechin gallate, epigallocatechin, gallic acid, epicatechin, dihydroquercetin, quercetin chalcone, 4,4'-dihydroxy-chalcone,

isoliquiritigenin, phloretin, coumestrol, 4',7-dihydroxy-flavanone, 4',5-dihydroxy-flavone, 4',6-dihydroxy-flavone, luteolin, galangin, equol, biochanin A, daidzein, formononetin, genistein, amentoflavone, bilobetin, taxifolin, delphinidin, malvidin, petunidin, pelargonidin, malonylapiin, pinosylvin, 3-methoxyapigenin, leucodelphinidin, dihydrokaempferol, apigenin 7-O-glucoside, pycnogenol, aminoflavone, purpurogallin fisetin, 2',3'-dihydroxyflavone, 3-hydroxyflavone, 3',4'-dihydroxyflavone, catechin, 7-flavonoxyacetic acid ethyl ester, catechin, hesperidin, naringin, deferoxamine, ergothioneine, heparin and combinations thereof.

161. (new) The method of claim 124 wherein said composition further comprises DMSO and mannitol.

162. (new) The method of claim 124 further comprising contacting the one or more tissues with trehalose.

163. (new) The method of claim 124 or 125 wherein said propylene glycol is a monomeric or polymeric glycol.

164. (new) The method of claim 163 wherein said polymeric glycol is polypropylene glycol 400 (PPG 400), PPG 1200 or PPG 2000.

165. (new) The method of claim 124 or 125 wherein said one or more tissues are packaged prior to said irradiation.

166. (new) A composition comprising one or more tissues prepared according to the method of claim 124 or 125.

167. (new) The composition of claim 166 wherein the composition further comprises one or more stabilizers selected from the group consisting of DMSO, mannitol and trehalose.

168. (new) A method for reducing the level of active biological contaminants or pathogens in one or more tissues, said method comprising contacting the tissue with a composition comprising propylene glycol, DMSO and mannitol and irradiating said one or more tissues with gamma radiation for a time effective to reduce the level of active biological contaminants or pathogens in said one or more tissues.

Summary of the Office Action

1. Claims 1 to 4, 15 to 17, 19 to 26, 28 to 30, 34, 35, 39 to 41, 50 to 52, 54 to 62, 66 to 69, 75, 77, 78, 82 to 92, 102 to 104, 108 to 110, 112 to 118 and 120 were rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Peterson (U.S. Patent 5,730,933).

2. Claims 1 to 4, 10 to 14, 28, 39, 42, 49, 54, 55, 64, 77, 79, 80 to 88, 93, 97, 101, 102, 104, 108 to 110 and 112-120 were rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Odland (U.S. Patent 5,989,498).

3. Claims 1, 27, 43 to 45 and 53 were rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Horowitz *et al.* (U.S. Patent 5,712,086).

4. Claims 5, 27 and 31 were rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Perterson in view of Horowitz *et al.*

5. Claims 6 to 9 were rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Peterson in view of Kent (U.S. Patent 6,171,549).

6. Claims 18 to 111 were rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Peterson.

7. Claims 32 and 33 were rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Peterson in view of Stieglitz (DE 3817603).

8. Claim 27 was rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Odland in view of Horowitz *et al.*

9. Claims 46 to 48 were rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Horowitz *et al.*

10. Claims 36-38, 63, 65, 70 to 74, 76, 94 to 96, 98 to 100, 105, 106 and 121 to 123 were objected to as being dependent upon a rejected base claim but would be allowable if rewritten in independent form to include all of the limitations of the base claim and any intervening claims.

Response to the Office Action

The Office Action dated March 3, 2004 has been carefully reviewed and the following amendments and comments are made in response. In view of the above amendments and following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims. Applicants respectfully submit that no new prohibited matter has been introduced by the claim amendments.

Claims 1 to 123 were pending and under examination. Claim 107 is allowed. Claims 1 to 106 and 108 to 123 have been cancelled without prejudice or disclaimer. After entry of the instant amendment, claims 107 and 124 to 168 will be pending.

Amendment to the Specification

The specification has been amended to insert a priority claim prior to line 1, page 1 of the specification. Applicants concurrently submit herewith a Petition for Unintentionally Delayed Claim under 37 C.F.R. 1.78. Applicants respectfully request that the Petition be granted and that the amendment to the specification be entered into the record.

Amendments to the Claims

Claims 124 to 168 have been added and are fully supported by the specification and claims as originally filed. Applicants respectfully submit that the substitute claims do not introduce new matter. While written description support for the substitute claims can be found throughout the specification and in the original claims, examples of specific support for the additional claims can be found in the original claims and specification as set forth in the table below.

Claim	Support in Specification and Original Claims
124, 125, 168	Page 10, paragraph 28; Page 14, paragraph 53; claims 2, 64, 65
126 to 130	Page 21, paragraph 61
131 to 133	Page 30, paragraph 93
134, 135	claim 15
136	Page 28, paragraph 87; claims 6, 13, 30
137 to 139	Page 29, paragraph 89
140 to 141	Page 40 to 41
142, 143	Page 41, paragraph 118
144 to 146	Page 57, paragraph 143
147, 148	claim 36
149	Page 31, paragraph 97
150 to 152	Page 19, paragraph 58
153	Page 27, paragraph 79
154	claims 21 to 25, 56 to 62
155	claim 63
157, 158	Page 20, paragraph 59

Claim	Support in Specification and Original Claims
159	Page 15, paragraph 54
160 to 162	Page 16, paragraph 57
163, 164	Page 15, paragraph 53
166, 167	claim 102

Rejection Under 35 U.S.C. 102(b)

Claims 1-4, 10-17, 19-30, 34, 39-45, 49, 50-62, 64, 66-69, 75, 77-88, 82-93, 97, 101-104, 108-110, 112-118 and 120 stand rejected under 35 U.S.C. 102(b) as allegedly anticipated by Peterson, Odland or Horowitz *et al.* Without acquiescing to the merits of the rejection, Applicants have cancelled these claims rendering the rejection moot. Substitute claims 124 to 168 all provide the limitation that propylene glycol be present in the claimed method or composition. As the Examiner has previously indicated that methods incorporating propylene glycol constitute allowable subject matter (see Office Action at page 7, item 16), Applicants submit that the cited references are not applicable as prior art against the substitute claims because they do not disclose all the limitations of the substitute claims.

Rejection Under 35 U.S.C. 103

Claims 5-9, 18, 27, 31-33, 46-48 and 111 stand rejected as allegedly being obvious under 35 U.S.C. 103. Without acquiescing to the merits of the rejection, Applicants have cancelled these claims rendering the rejection moot. As mentioned above, substitute claims 124 to 168 all provide the limitation that propylene glycol be present in the claimed method or composition. As the Examiner has previously indicated that methods incorporating propylene glycol constitute allowable subject matter (see Office Action at page 7, item 16), Applicants submit that the cited references do not disclose nor suggest all the limitations of the substitute claims.

Conclusion

Applicants respectfully request reconsideration of the subject application in view of the substitute claims and the above remarks. It is respectfully submitted that this application is now in condition for allowance. Should the Examiner believe it to be useful, an interview with the Examiner is respectfully requested in order to discuss the foregoing claims.

Except for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application, including fees due

under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **constructive petition for extension of time** in accordance with 37 C.F.R. 1.136(a)(3).

Dated: **June 8, 2004**
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